Hispidin-3-hydroxylase: a luciferin biosynthesis enzyme of glowing fungi

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Bioluminescence is on the front edge of biological sciences both as a fundamental research topic and as a tool for different applications. Despite the fact that this topic is being extensively researched none genetically encodable eukaryotic bioluminescent systems are known. Our research group has recently established the structure of fungal luciferin: 3-hydroxyhispidin, a derivative of a known secondary metabolite hispidin ((E)-6-(3,4-dihydroxystyril)-4-hydroxy-2H-pyran-2-on). During the past year we have also found two novel enzymes: luciferase and hispidin-3-hydroxylase (H3H) from the bioluminescent fungus Neonothopanus nambi. The second enzyme catalyzes hydroxylation of hispidin and is a key enzyme of fungal luciferin biosynthesis. Using a bioinformatics approach we identified close H3H homologues in other bioluminescent fungi, e.g. Pannella stipitata, Mycena cytricolor, Armillaria mellea. We also proved experimentally the function of H3H in heterologous expression systems, such as yeast Pichia pastoris, bacteria and mammalian cell cultures. Moreover, we have constructed functional chimeric fusion proteins, containing both luciferase and H3H. We believe that our work is a first and important step towards the development of the first fully genetically encodable eukaryotic bioluminescence system.

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